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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,120	11/29/2004	Masaru Yamakoshi	1516-0126PUS1	3292

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EXAMINER	
MARTIN, PAUL C	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	01/05/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/05/2007.

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mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,120	YAMAKOSHI ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18-21 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,18-21 and 24-29* is/are rejected.

7)☒ Claim(s) *10-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14, 18-21 and 24-29 are pending in this application and were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 07/20/06 in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The objections to Claims 5-15, 25, 26 and 28 under 37 C.F.R. § 1.75(c) as being in improper form has been withdrawn due to the Applicant's amendments to the Claims filed 09/20/06.

Claim Rejections - 35 USC § 102

Claim 1 remains rejected under 35 U.S.C. 102(b) as being anticipated by Larner (5,750,348) for reasons of record set forth in the Action mailed 04/20/06.

The rejection of Claims 1-4 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ashizawa *et al.* (2000) has been withdrawn due to the Applicant's amendments to the Claims filed 09/20/06.

Response to Arguments

Applicant's arguments filed 09/20/06 have been fully considered but they are not found to be persuasive.

The Applicant argues that "insulin resistance", "mild impaired glucose tolerance" and "insulin secretory defect", are different terms relating to different biochemical problems, and that "mild impaired glucose tolerance" represents a new classification (Remarks, Pg. 10, Lines 5-10).

The Applicant argues that Larner discloses a method of screening for insulin resistance or type II diabetes and not "mild impaired glucose tolerance" or a "secretory defect" as in instant Claim 1 (Pg. 10, Lines 18-22).

The Applicant's arguments are not found to be persuasive for the following reasons, the method of Larner inherently anticipates the instantly claimed invention in the following manner; the method of Larner for measuring myoinositol from subjects and relating the levels of myoinositol as a marker or predictor of insulin resistance and of type II diabetes performs the same steps as described in Claim 1. The fact that Applicant has chosen to define a narrow point between "normal" and "insulin resistance/glucose tolerance" is of no functional relevance to the method as claimed.

Larner teaches providing urine samples from human subjects, quantitatively determining the myoinositol levels in the samples, and determining whether the subjects are insulin resistant or have type II diabetes (characterized by insulin resistance) if the concentration of myoinositol is higher than a normal value. The relationship of these values to the arbitrary classifications as defined by the instant application constitute mental steps on the part of the Applicant and do not materially change the fact that Larner anticipates the method steps of instant claim 1.

Claim Rejections - 35 USC § 103

The rejection of Claims 1-4, 18-20 and 27 under 35 U.S.C. 103(a) as being unpatentable over Ashizawa *et al.* (2000) in view of Tazoe *et al.* (6,309,852) has been withdrawn due to the Applicant's amendments to the Claims filed 09/20/06.

Claims 1-5 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Larner (US 5,750,348) in view of Ashizawa *et al.* (2000).

The teachings of Larner and Ashizawa *et al.* were discussed in the previous action.

It would have been obvious to one of ordinary skill in the art to combine the method for detecting insulin resistance or type II diabetes by quantitatively determining myo-inositol levels in urine samples using Gas Chromatograph/Mass Spectroscopy (GC/MS) and evaluating cases where the level shows a characteristic value higher than normal as insulin resistant or type II diabetic as taught by Larner, with the method for quantitatively determining myo-inositol in rat tissue samples using the enzyme myo-inositol dehydrogenase and NADH in an enzymatic cycling method of Ashizawa *et al.* because one of skill in the art would have recognized that the quantitative determinations of myoinositol using GC/MS would be a functional equivalent technique of the enzymatic determination of myoinositol as taught by Ashizawa *et al.* previously. One of ordinary skill in the art would have been motivated to combine these two methods because the use of alternatives and functional equivalent techniques would have been desirable to those of ordinary skill in the art based upon the economics and availability of compounds. There would have been a reasonable expectation of success in making this adaptation because both methods are drawn to techniques for the quantitative determination of myoinositol in mammalian biological samples.

Claims 1-7, 19, 20 and 27-29 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Larner (US 5,750,348) in view of Ashizawa *et al.* (2000) as applied to Claims 1-5 above and further in view of Tazoe *et al.* (6,309,852).

The teachings of Larner, Ashizawa *et al.*, and Tazoe *et al.* were discussed in a previous action.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods for quantitatively determining the amount of myo-inositol in a sample using ATP-hexokinase to remove interfering glucose as taught by Larner and Ashizawa *et al.* with the method of eliminating glucose interference using two kinds of kinase, one of which being ADP-dependent hexokinase as taught by Tazoe *et al.* in order to remove the possible interference of glucose and ADP on the reaction. One of ordinary skill in the art would have been motivated to combine the two methods in order to achieve the dual advantages of removing glucose interference by two overlapping means and simultaneously removing potentially interfering ADP accumulations as taught by Tazoe *et al.* above. There would have been a reasonable expectation of success based upon the fact that both methods use hexokinase and are drawn toward eliminating glucose interference and examining markers for glucose intolerance or insulin secretion defect markers.

Response to Arguments

Applicant's arguments filed 09/20/06 have been fully considered but they are not found to be persuasive.

The Applicant argues that Ashizawa *et al.* does not teach each and every limitation of claims 1-4 regarding determination of "mild impaired glucose tolerance" (Remarks, Pg. 14, Lines 17-20 and Pg. 15, Lines 1-2).

This is not found persuasive due to the reasoning applied in the new obviousness type rejection of Claims 1-4 over Larner and Ashizawa *et al.* above.

The Applicant argues that Ashizawa *et al.* disclose the use of ATP-hexokinase to eliminate glucose generating glucose-6-phosphate and ADP, but does not suggest a method to further eliminate the ADP (Pg. 15, Lines 16-18), and further that Tazoe *et al.* do not disclose or suggest the elimination of ADP from the reaction system (Remarks, Pg. 17, Lines 17-22).

This is not found to persuasive because Tazoe *et al.* clearly recognizes that when glucose is eliminated by the use of hexokinase, that unfavorable amounts of ADP are formed (Column 1, Lines 59-67), and further clearly teaches that when the enzyme acting on the analyte also acts on glucose and the reaction catalyzed by the enzyme is subject to influence of the NDP concentration, it is preferred to eliminate glucose using system A in which the enzyme is NDP-dependent hexokinase and the coenzyme is NDP converted to NMP (Column 6, Lines 23-28). Further, Tazoe *et al.* definitively teaches the elimination of glucose from a reaction through the simultaneous use of NTP-dependent hexokinase to facilitate the reaction of glucose and NTP to glucose-6-phosphate and NDP and the reaction of NDP with NDP-dependent hexokinase to form NMP (Column 5, Lines 14-22).

The Applicant argues that the inventors have attempted the method of Tazoe *et al.* unsuccessfully (Remarks, Pg. 18, Lines 15-17) and that the instantly invention removes glucose at an unexpectedly higher rate than does the method of Tazoe *et al.* (Remarks, Pg. 18, Lines 17-22).

The fact that the Applicants have attempted the method of Tazoe *et al.* unsuccessfully to remove the interference by glucose, is not relevant to the issue at hand as Tazoe *et al.* is an issued US Patent, and thus, is presumed to be enabled.

Applicant has not submitted any conclusive data or evidence to bear out the allegation of unexpected results over the prior art, and therefore the argument is not found persuasive.

Claims 1-9, 18-21 and 24-29 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Larner (US 5,750,348) in view of Ashizawa *et al.* (2000) and Tazoe *et al.* (6,309,852) as applied to Claims 1-7, 18-20 and 27-29 above and further in view of Kozuma *et al.* (US 6,046,018).

The teachings of Larner, Ashizawa *et al.* and Tazoe *et al.* were discussed above.

Neither Larner, Ashizawa *et al.* nor Tazoe *et al.* teach the use of thio-NAD.

Kozuma *et al.* teaches a method for the quantitative determination of chiro-inositol (a marker for insulin resistance) in a sample enzymatically using a dehydrogenase, in the presence of thio-NAD (Column 1, Lines 1-50) and the use of thio-NAD as a coenzyme at a final concentration of 2.0mM (Column 17, Line 56).

Kozuma *et al.* teaches that previously known myo-inositol and inositol dehydrogenases would not catalyze reaction using thio-NAD and thus would not be useful for enzyme cycling reactions using NAD and thio-NAD (Column 2, Lines 28-45), and teaches a new inositol dehydrogenase that will catalyze thio-NAD and NAD (Column 3, Lines 4-26).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the method for quantitatively determining the amount of myo-inositol in a sample using myoinositol dehydrogenase, ATP-hexokinase and ADP-hexokinase to remove interfering glucose as taught by Larner, Ashizawa *et al.* and Tazoe *et al.* with the use of thio-NAD as a coenzyme as taught by Kozuma *et al.* because one of skill in the art would have recognized that thio-NAD was a functional equivalents of the coenzymes NDP and NTP. One of ordinary skill in the art at the time of invention would have been motivated to combine the methods in order to achieve the advantages described by Kozuma *et al.* above, such as being able to use a new inositol dehydrogenase that will catalyze thio-NAD and NAD. There would have been a reasonable expectation of success based on the similarity between the enzymatic cycling methods (being drawn to characterizing diabetes markers) and their overlapping use of similar materials.

Response to Arguments

The Applicant argues that the combination of the disclosures of Ashizawa *et al.* and Tazoe *et al.* and Kozuma *et al.* do not disclose the compositions of Claims 21 and 24 and that the combination of Ashizawa *et al.* with Tazoe *et al.* does not suggest a combination of myo-inositol dehydrogenase with ATP-hexokinase and ADP-hexokinase.

This is not found to be persuasive due to the reasoning above, wherein the combined references of Larner, Ashizawa *et al.* and Tazoe *et al.* are shown to disclose the compositions of Claims 21 and 24 and motivation to combine the references is provided above.

Conclusion

Claims 10-14 appear to be free of the art, however the claims are objected to as being dependent upon rejected Claims 1 and 2.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/22/06

JON WEBER
SUPERVISORY PATENT EXAMINER